

5 We claim:

1. A composition comprising a tissue adherent hydrogel comprising an anti-arrhythmic agent and an anti-inflammatory for local delivery to a patient in need thereof.
2. The composition of claim 1 wherein the hydrogel is formed by
10 polymerization of biocompatible, biodegradable, synthetic, water soluble and covalently reactive macromers.
3. The composition of claim 1 wherein the anti-arrhythmic agent is selected from the group consisting of sodium channel blockers, beta-adrenergic blockers, repolarization prolonging agents, and calcium channel
15 blockers.
4. The composition of claim 3 wherein the anti-arrhythmic agent is selected from the group consisting of lidocaine, moricizine, mexiletine, tocainide, procainamide, encainide, flecanide, tocainide, phenytoin, propafenone, quinidine, disopyramide, flecainide, propranolol, esmolol,
20 amiodarone, artilide, bretylium, clofilium, isobutilide, sotalol, azimilide, dofetilide, dronedarone, ersentilide, ibutilide, tedisamil, trecetilide, verapamil, diltiazem, digitalis, adenosine, nickel chloride, and magnesium.
5. The composition of claim 3 wherein the anti-arrhythmic agent is a repolarization prolonging agent.
- 25 6. The composition of claim 5 wherein the anti-arrhythmic agent is selected from the group consisting of amiodarone, sotalol and dronedarone.
7. The composition of claim 6 wherein the anti-arrhythmic agent is amiodarone.
8. The composition of claim 1 wherein the anti-arrhythmic agent is
30 present in a dosage which is sufficient to produce a therapeutically effective level of the agent in the cardiac tissue for at least four days after implantation.
9. The composition of claim 1 wherein the anti-arrhythmic agent is poorly soluble in water.
- 35 10. The composition of claim 1 wherein the anti-arrhythmic agent is in nanoparticulate form precipitated within the hydrogel.

- 5 11. The composition of claim 1 wherein the anti-arrhythmic agent is encapsulated in a biodegradable material and suspended in the hydrogel.
12. The composition of claim 1 wherein the hydrogel is polymerized *in vitro* with the drug to form a hydrogel patch, prior to administration to a tissue.
- 10 13. The composition of claim 1 comprising a diacrylated polyethylene oxide comprising biodegradable linkages selected from the group consisting of monomers and oligomers of carbonates and hydroxyacids, polymerized to form a hydrogel degrading in a period following application to tissue which minimizes tissue inflammation or
- 15 fibrosis, and amiodarone in a dosage effective to lengthen atrial effective refractory period.
14. The composition of claim 1 in a kit further comprising means for increasing adhesion of the hydrogel to tissue.
15. The composition of claim 14 wherein the means for increasing
- 20 adhesion is biocompatible, biodegradable, synthetic, water soluble and covalently reactive macromers polymerizable to form an adhesive between the hydrogel and tissue.
16. The composition of claim 1 further comprising a viscosity modifying agent.
- 25 17. The composition of claim 16 wherein the viscosity modifying agent is selected from the group consisting of glycosaminoglycans, carboxymethyl cellulose, dextran, dextran sulfate, and polyvinylpyrrolidone.
18. A solution comprising biocompatible, biodegradable, synthetic, water soluble and covalently reactive macromers polymerizable to form a
- 30 tissue adhesive hydrogel degrading in a period of less than one month after application to the tissue, an anti-inflammatory agent, and an anti-arrhythmic agent in a dosage effective to lengthen atrial effective refractory period.
19. The solution of claim 18 comprising a diacrylated polyethylene oxide comprising biodegradable linkages degrading in a period of less than
- 35 about two weeks following application to the tissue.

5 20. The solution of claim 19 wherein the biodegradable linkages are selected from the group consisting of carbonate monomers and hydroxy acids.

 21. The solution of claim 18 wherein the anti-arrhythmic agent is selected from the group consisting of lidocaine, moricizine, mexiletine,
10 tocainide, procainamide, encainide, flecanide, tocainide, phenytoin, propafenone, quinidine, disopyramide, flecainide, propranolol, esmolol, amiodarone, artilide, bretylium, clofilium, isobutilide, sotalol, azimilide, dofetilide, dronedarone, ersentilide, ibutilide, tedisamil, trecetilide, verapamil, diltiazem, digitalis, adenosine, nickel chloride, and magnesium.

15 22. The solution of claim 18 wherein the anti-arrhythmic agent is selected from the group consisting of amiodarone, sotalol and dronedarone.

 23. The solution of claim 22 comprising macromers comprising a diacrylated polyethylene oxide comprising biodegradable linkages selected from the group consisting of monomers and oligomers of carbonates and
20 hydroxyacids, polymerizable to form a hydrogel degrading in a period following application to tissue which minimizes tissue inflammation or fibrosis, and amiodarone in a dosage effective to lengthen atrial effective refractory period.

 24. The solution of claim 18 in a kit further comprising reagents for
25 priming the surface of the tissue to which the solution is to be applied, wherein the priming increases the adhesion of the hydrogel to the tissue.

 25. The solution of claim 18 further comprising a viscosity modifying agent.

 26. The solution of claim 25 wherein the viscosity modifying agent
30 is selected from the group consisting of glycosaminoglycans, carboxymethyl cellulose, dextran, dextran sulfate, and polyvinylpyrrolidone.

 27. A method for delivering an anti-arrhythmic agent, comprising topically applying to the surface of cardiac tissue or blood vessels an anti-arrhythmic agent and an anti-inflammatory agent dispersed in a
35 hydrogel, or a solution forming a hydrogel.

 28. The method of claim 27 comprising

5 administering to the surface of cardiac tissue or blood vessels a
solution of biocompatible, biodegradable, synthetic, water soluble and
covalently reactive macromers comprising the anti-arrhythmic agent, and
polymerizing the macromer solution to form a tissue adherent
hydrogel.

10 29. The method of claim 27 comprising
administering to the surface of cardiac tissue or blood vessels a hydrogel
formed of biocompatible, biodegradable, synthetic, water soluble and
covalently reactive macromers comprising the anti-arrhythmic agent to be
delivered.

15 30. The method of claim 27 wherein the anti-arrhythmic agent is
selected from the group consisting of sodium channel blockers, beta-
adrenergic blockers, repolarization prolonging agents, and calcium channel
blockers.

20 31. The method of claim 30 wherein the anti-arrhythmic agent is
selected from the group consisting of lidocaine, moricizine, mexiletine,
tocainide, procainamide, encainide, flecanide, tocainide, phenytoin,
propafenone, quinidine, disopyramide, flecainide, propranolol, esmolol,
amiodarone, artilide, bretylium, clofilium, isobutilide, sotalol, azimilide,
dofetilide, dronedarone, ersentilide, ibutilide, tedisamil, trecetilide,
25 verapamil, diltiazem, digitalis, adenosine, nickel chloride, and magnesium.

32. The method of claim 30 wherein the anti-arrhythmic agent is a
repolarization prolonging agent.

33. The method of claim 32 wherein the anti-arrhythmic agent is
selected from the group consisting of amiodarone, sotalol and dronedarone.

30 34. The method of claim 33 wherein the anti-arrhythmic agent is
amiodarone.

35 35. The method of claim 34 wherein the hydrogel comprises a
diacrylated polyethylene oxide comprising biodegradable linkages selected
from the group consisting of monomers and oligomers of carbonates and
hydroxyacids, polymerized to form a hydrogel degrading in a period
following application to tissue which minimizes tissue inflammation or

5 fibrosis, and amiodarone in a dosage effective to lengthen atrial effective refractory period.

36. The method of claim 27 further comprising applying to the tissue means for increasing adhesion of the hydrogel to tissue.

10 37. The method of claim 36 wherein the means for increasing adhesion is biocompatible, biodegradable, synthetic, water soluble and covalently reactive macromers polymerizable to form an adhesive between the hydrogel and tissue.

38. The method of claim 27 wherein the anti-arrhythmic agent is present in a dosage effective to lengthen atrial effective refractory period.

15 39. The method of claim 27 in which the therapeutically effective level is maintained for at least four days after implantation.

40. The method of claim 27 wherein the hydrogel degrades over a period of time of two weeks or less.

20 41. The method of claim 27 further comprising administering a viscosity modifying agent in the solution forming the hydrogel.

42. The method of claim 41 wherein the viscosity modifying agent is selected from the group consisting of glycosaminoglycans, carboxymethyl cellulose, dextran, dextran sulfate, and polyvinylpyrrolidone.

25 43. The composition of claim 1, wherein the anti-inflammatory agent is dexamethasone or dexamethasone acetate.

44. The solution of claim 18, wherein the anti-inflammatory agent is dexamethasone or dexamethasone acetate.

45. The method of claim 27, wherein the solution further comprises dexamethasone or dexamethasone acetate.